Armed Forces College of Medicine

AFCM

Viral Lower Respiratory tract infections (Part 2)

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INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1.Describe the structure and antigenecity of viruses causing LRTIs

2.Describe pathogenesis and clinical manifestationsof viral LRTIs

3. Outline laboratory diagnosis of viral LRTIs.

Respiratory Tract Infections

Upper respiratory tract Diseases

- **Common Cold**
- **Pharyngitis**
- Otitis Media
- Sinusitis
- **Laryngitis**
- Epiglottitis

Upper and Lower respiratory Tract Diseases

- **Croup**
- **Influenza**
- Whooping Cough

Lower Respiratory Tract Diseases

- **Bronchitis**
- **Bronchiolitis**
- **Pneumonia**
- Pulmonary TB
- Lung Abscess

PNEUMONIA

Definition

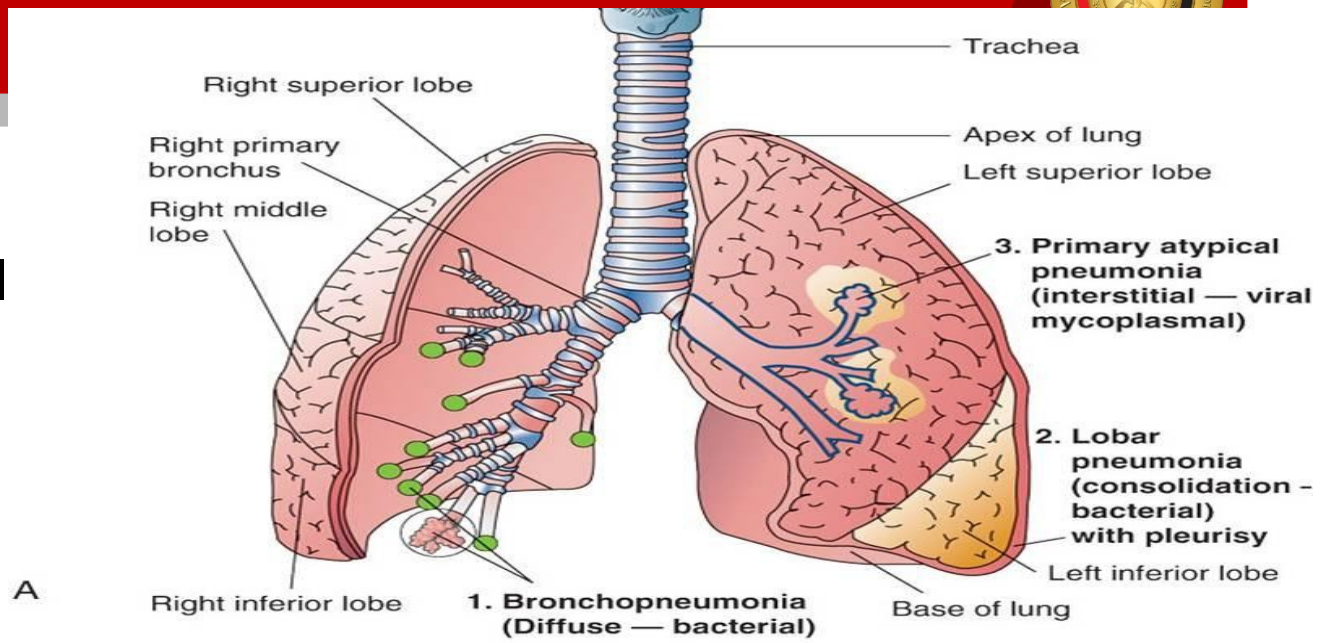
Inflammation of the **lung affecting the al**

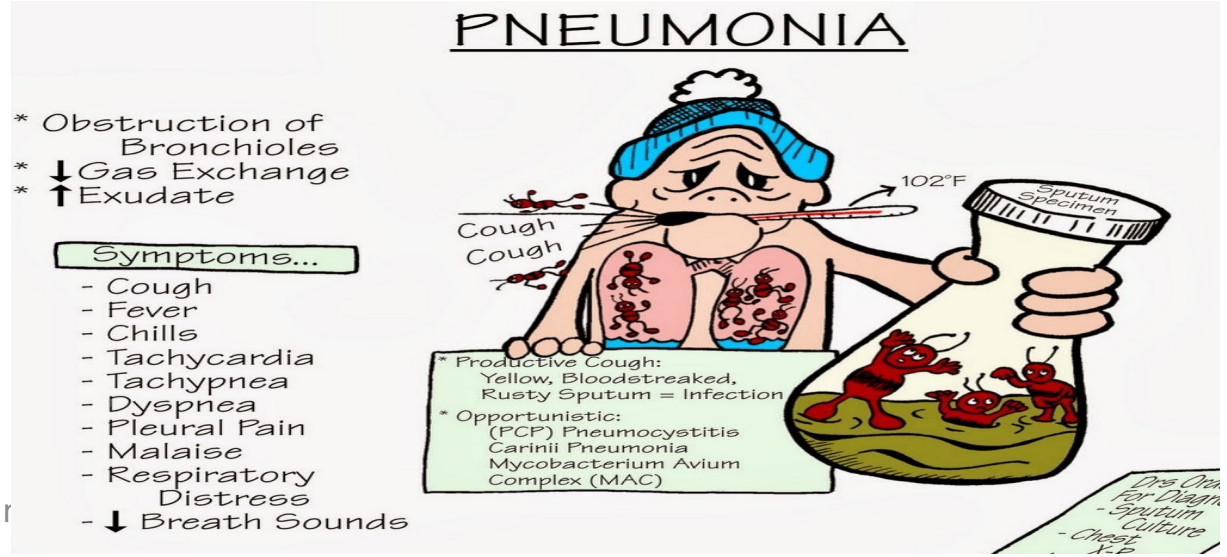
Clinical manifestations

1-Fever & Chest pain

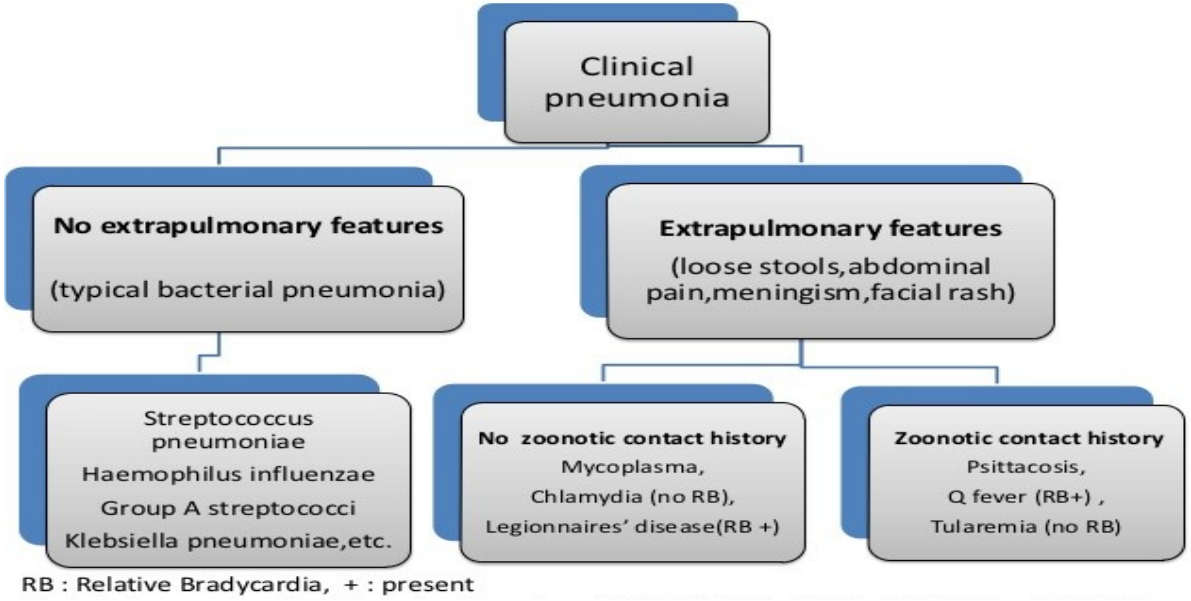
2-Cough (dry or productive)

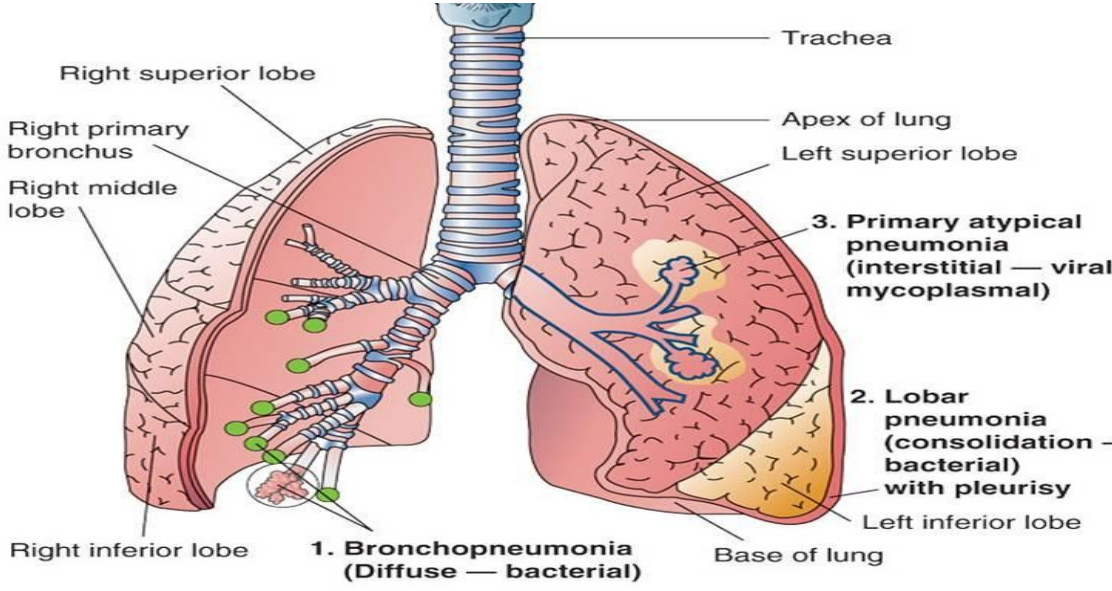
3-Dyspnea





Clinical classification	
Typical	Atypical
Manifestations	
1-Rapid onset 2-More severe symptoms 3-Productive cough 4-Dense consolidation on chest Xray 5-Causative organism can be isolated on routine culture media	**1-Slower onset** **2-Less severe symptoms** **3-Nonproductive cough** **4-Patchy interstitial pattern on chest X ray.** **5-Causative organisms can't be isolated on routine culture media**
Causative agents	
1-Strept.pneumoniae. 2-H.influenzae 3-Pseudomonas aeruginosa. 4-Klebsiella pneumoniae.	1-Legionella pneumophilla 2-Mycoplasma pneumoniae. 3-Chlamydia pneumoniae.& psittaci. 4-Coxiella burnetti. **5-Viruses and fungi.**





Viral causes of Atypical Pneumonia

1-Influenza virus: the most common cause .

2-Respiratory syncitial virus.

3-Adenovirus.

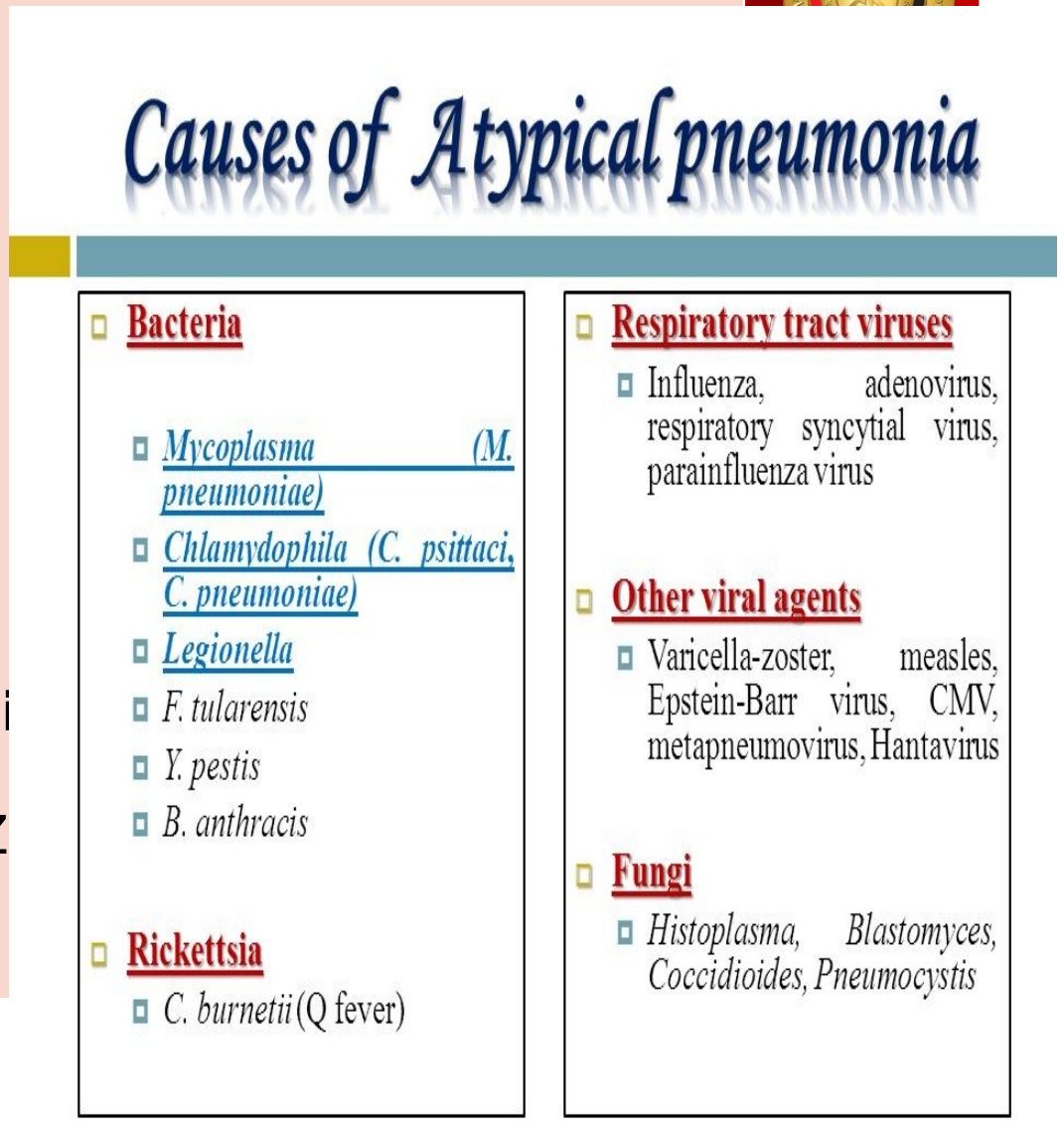
4- Corona viruses

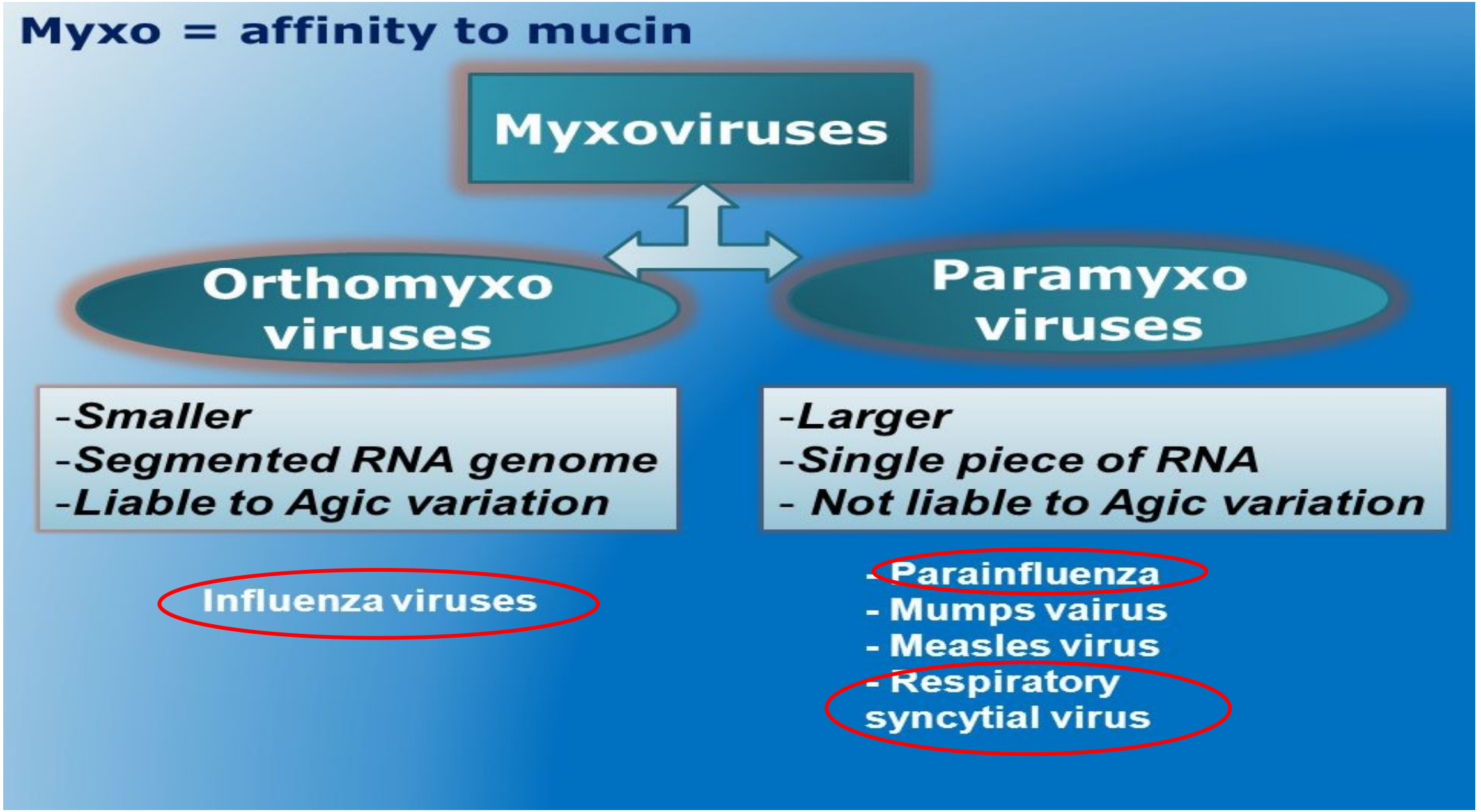
SARS -Cov ,MERS-Cov &SARS -Cov -2

5-Herpes viruses : in patients with ↓ cell medi

Cytomegalovirus,Herpes simplex virus & Varicella Z

6-Hanta virus : in certain geographical areas




Myxo = affinity to mucin
Myxoviruses
Orthomyxo viruses
Paramyxo viruses
-Smaller
-Segmented RNA genome
-Liable to Agic variation
-Larger
-Single piece of RNA
- Not liable to Agic variation
Influenza viruses
- Parainfluenza
- Mumps vairus
- Measles virus
- Respiratory syncytial virus

Influenza Viruses

Structure

A- Family

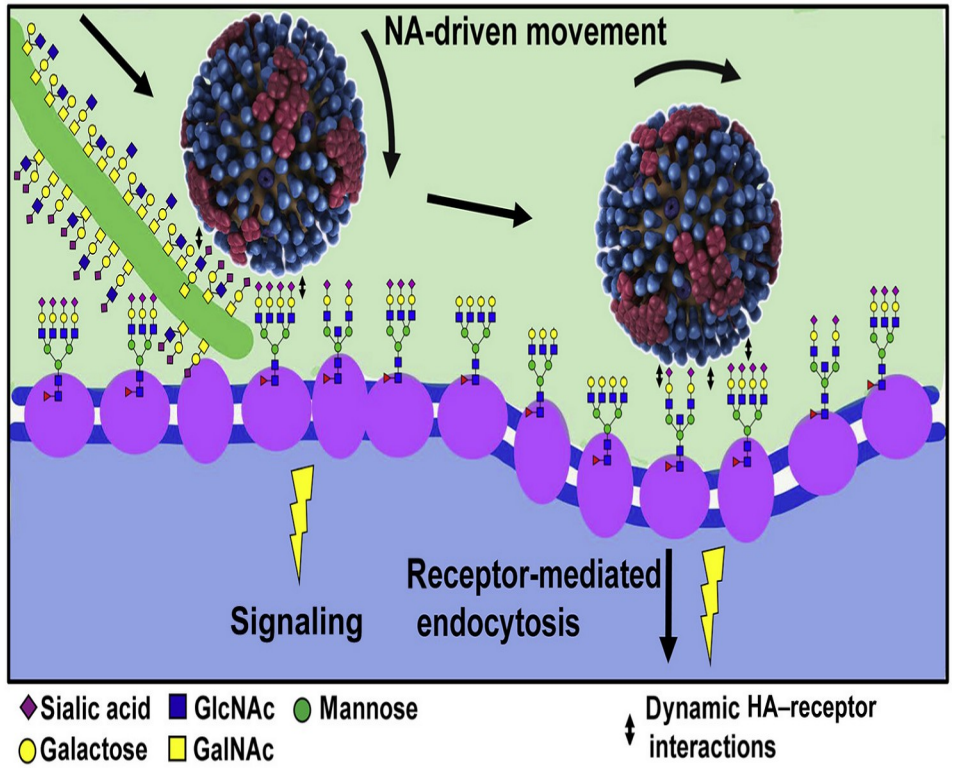
Are the only members of the **orthomyxoviruses**

(**myxo** *:* interact with **mucins;**

glycoproteins on the surface of cells).

- They replicate in **mucous membranes**

of upper and lower respiratory tract.



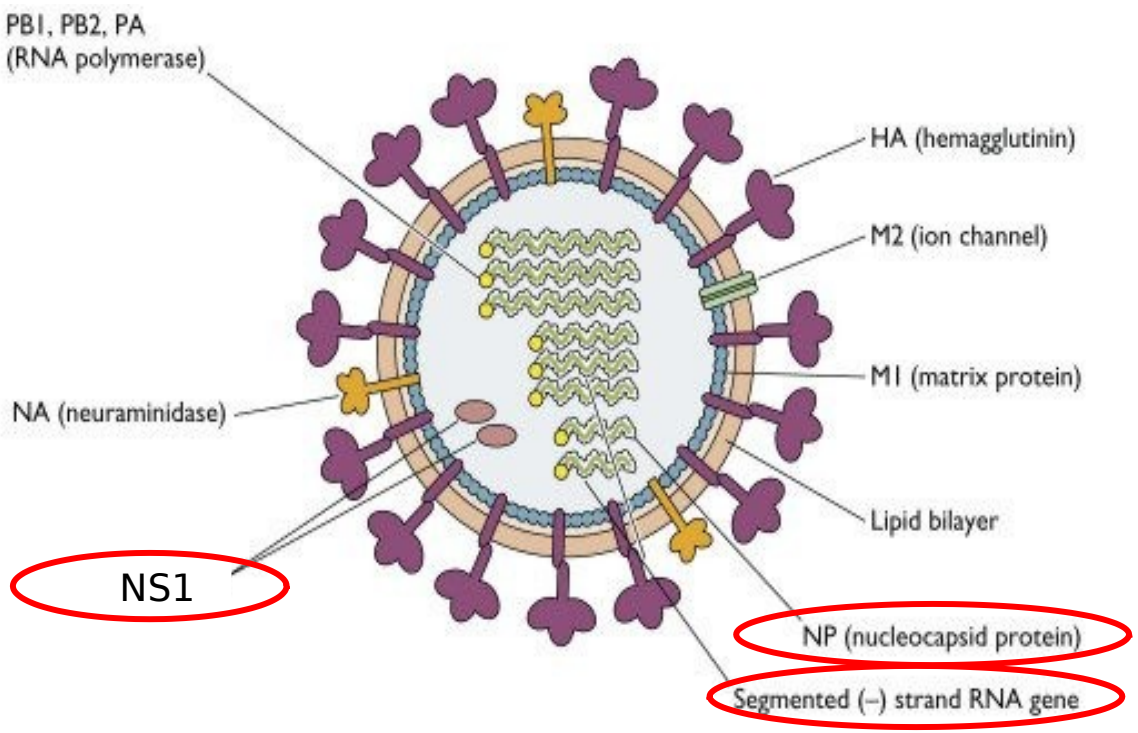
B-Nucleocapsid

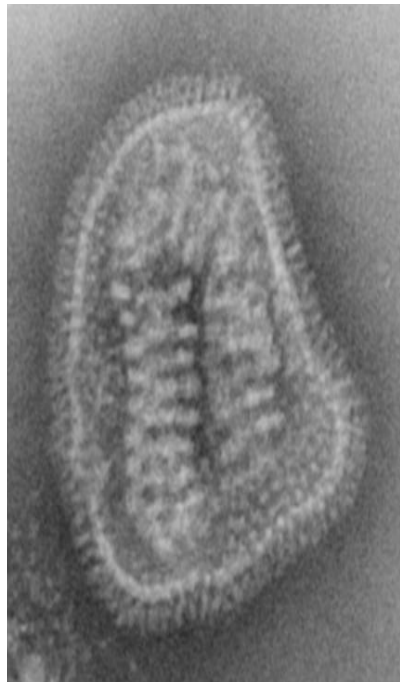
1- Segmented ssRNA genome :

8 segments

2-Helical

3-Group (type) specific Ags





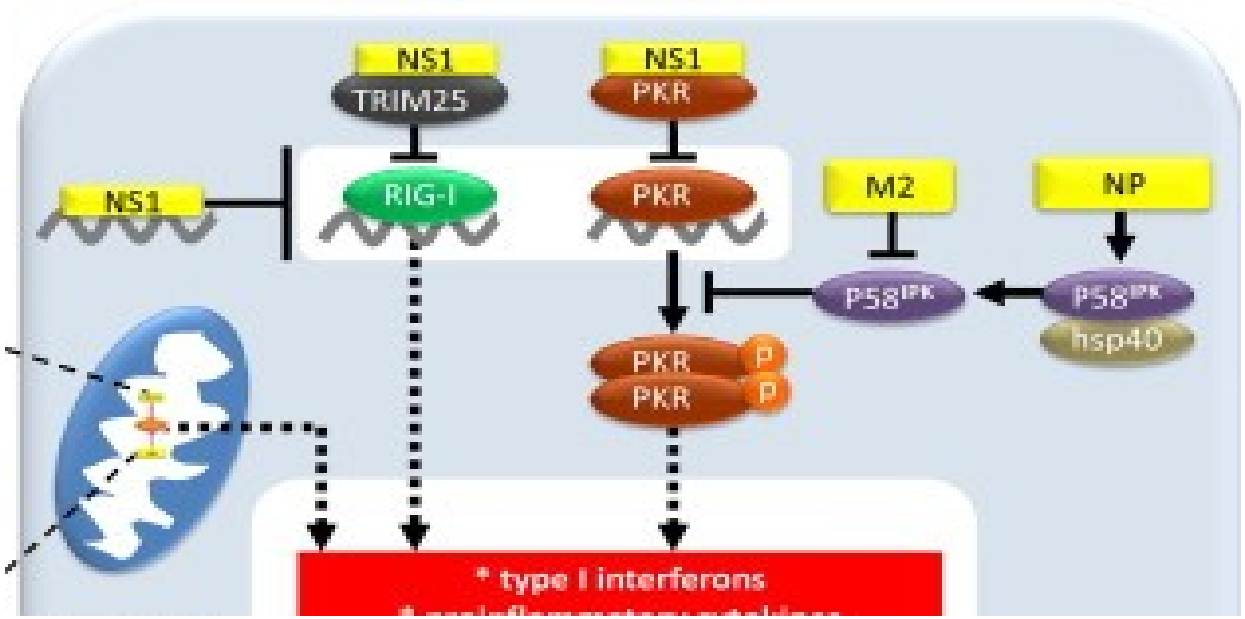
Internal ribonucleoprotein divides the virus

into **3 types: A,B &C**

4-Non structural protein : NS1

Inhibits production of Interferon

Enhances viral **virulence**



Influenza Viruses

C - Envelopel

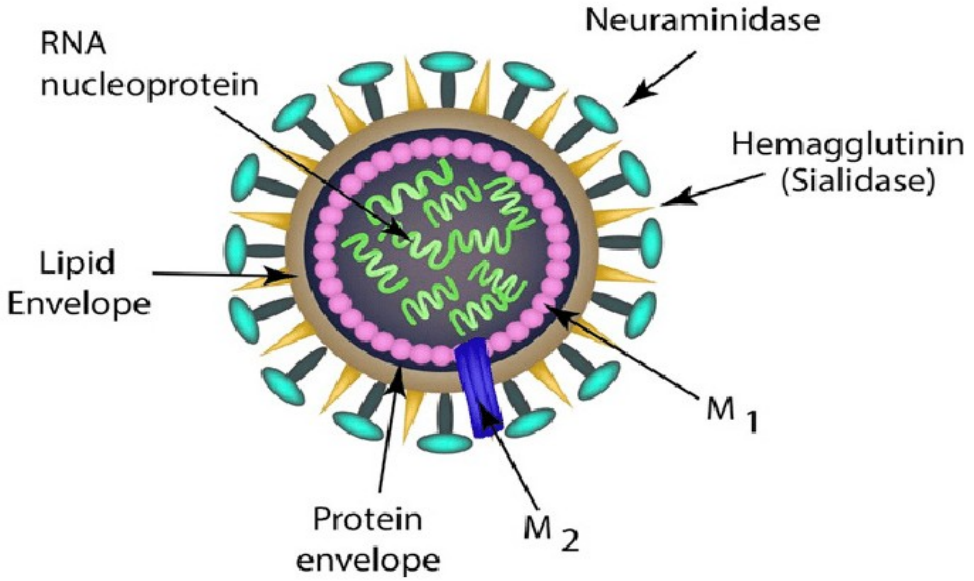
Contains **2 projecting glycoprotein spikes** :

Heamagglutinin(**HA) & Neuraminidase (NA)**

Subtype (strain) specific Ags (Major Ags)

; Divide type A into strains

Heamagglutinin (HA)



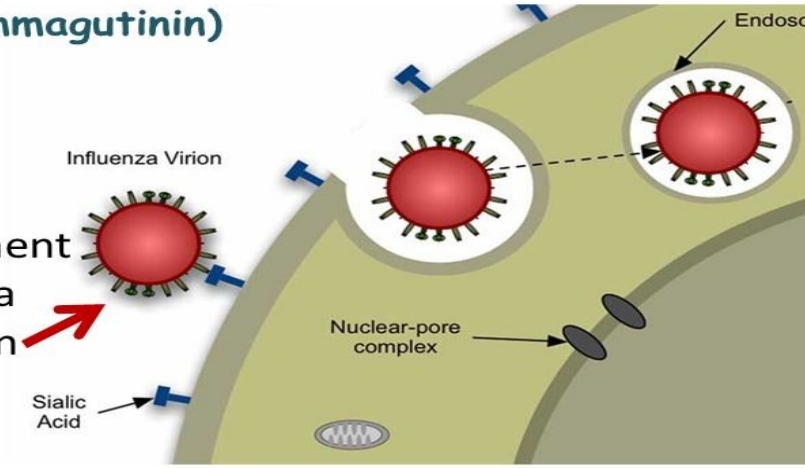
1-Binds to host cell **receptors**

Viral entry

Abs against it **neutralize infectivity & prevent disease**

2 - **Heamagglutination** of animal RBCs

N-Acetylneuraminic acid (Sialic acid) is the influenza virus receptor (hemmagutinin)



•Allowing attachment to mucous cells via viral hemagglutinin (HA)

Neuraminidase (NA)

1- **Cleaves neuraminic acid** of infecte

↓

Viral **release** (at end of infection)

↓

Abs against it ↓ **viral release & s**

2 - **Degrade protective mucus** in RT

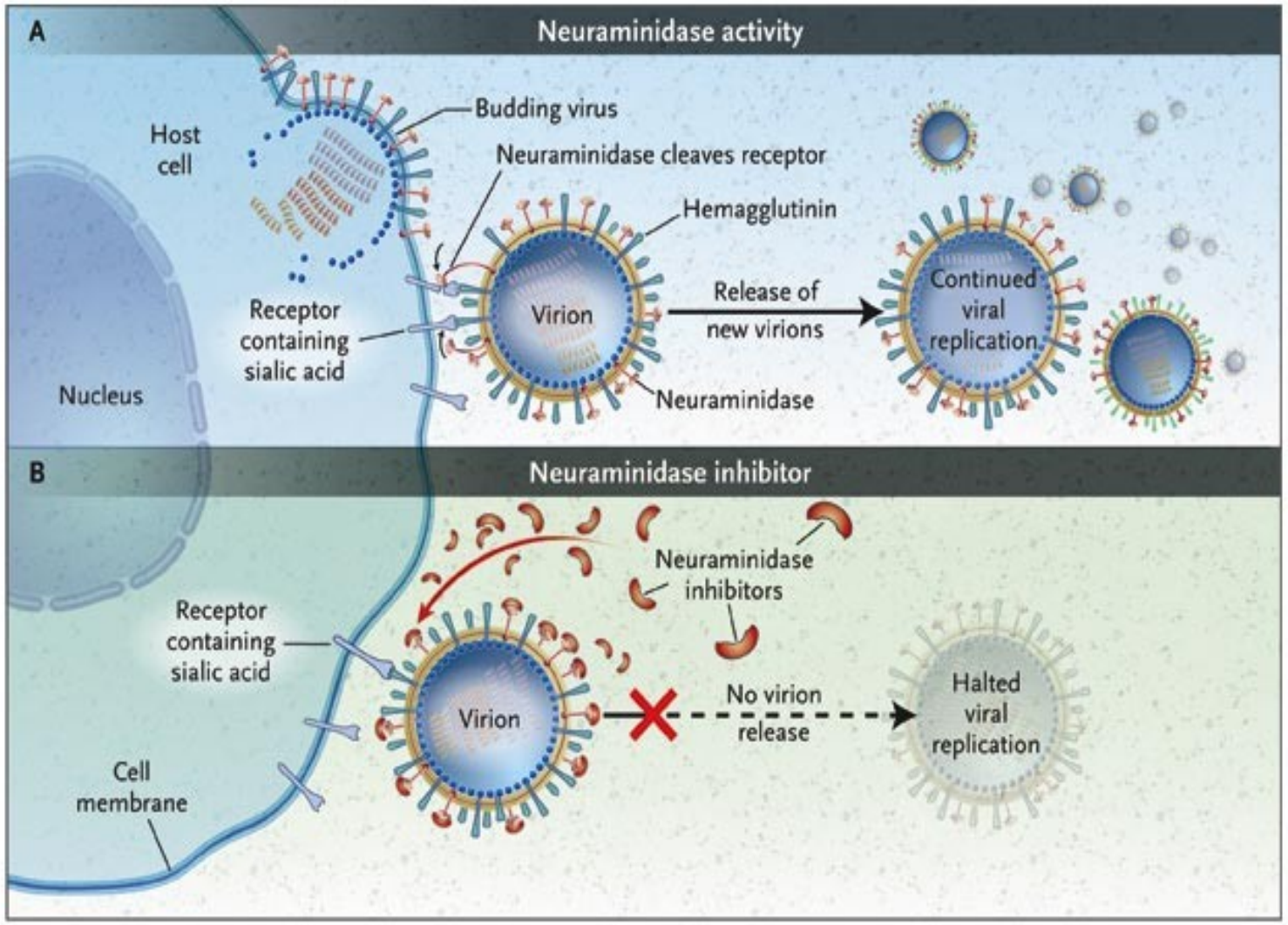
↓

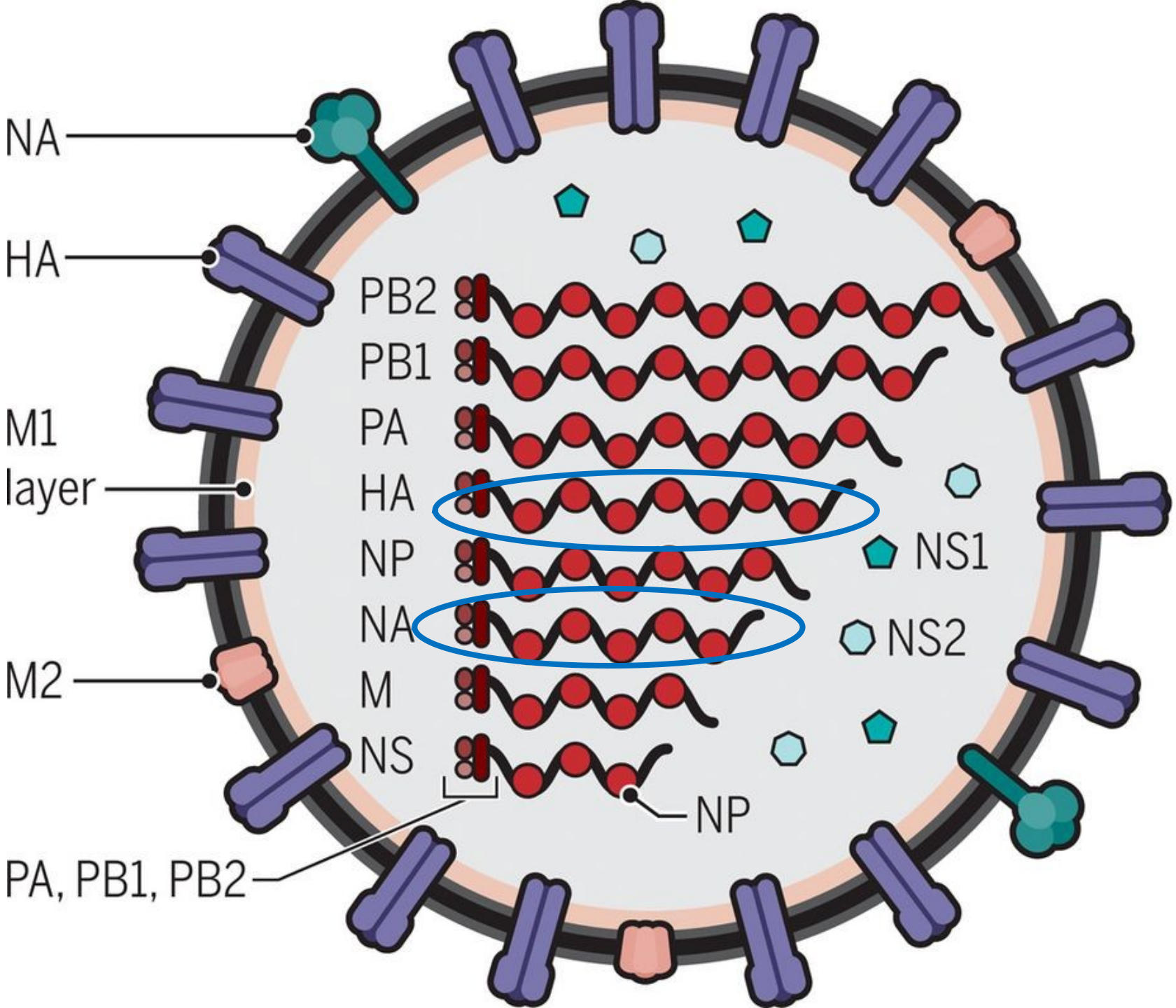
Virus **gets access to epithelial cells**

(at beginning of infection)

NA is inhibited by

Oseltamivir (Tamiflu)





Accessory proteins

PB1-F2

M42

PA-X

M3*

M4*

NS3*

NSP*

*Putative

Classification of Influenza viruses

Influenza viruses have **Type -specific** and **subtype(strain)-specific antigens.**

Internal ribonucleoproteins — **Hemagglutinin and Neuraminidase**

Influenza A

- Has 18 different types Haemagglutinin (H1 to H18) &

  11 different Neuraminidase (N1 to N11)

Each strain is named according to **its type of HA &NA e.g.**

H1N1

- **Infects human & other species**

  Many species of animals (e.g., aquatic birds, chickens, swine, and hc

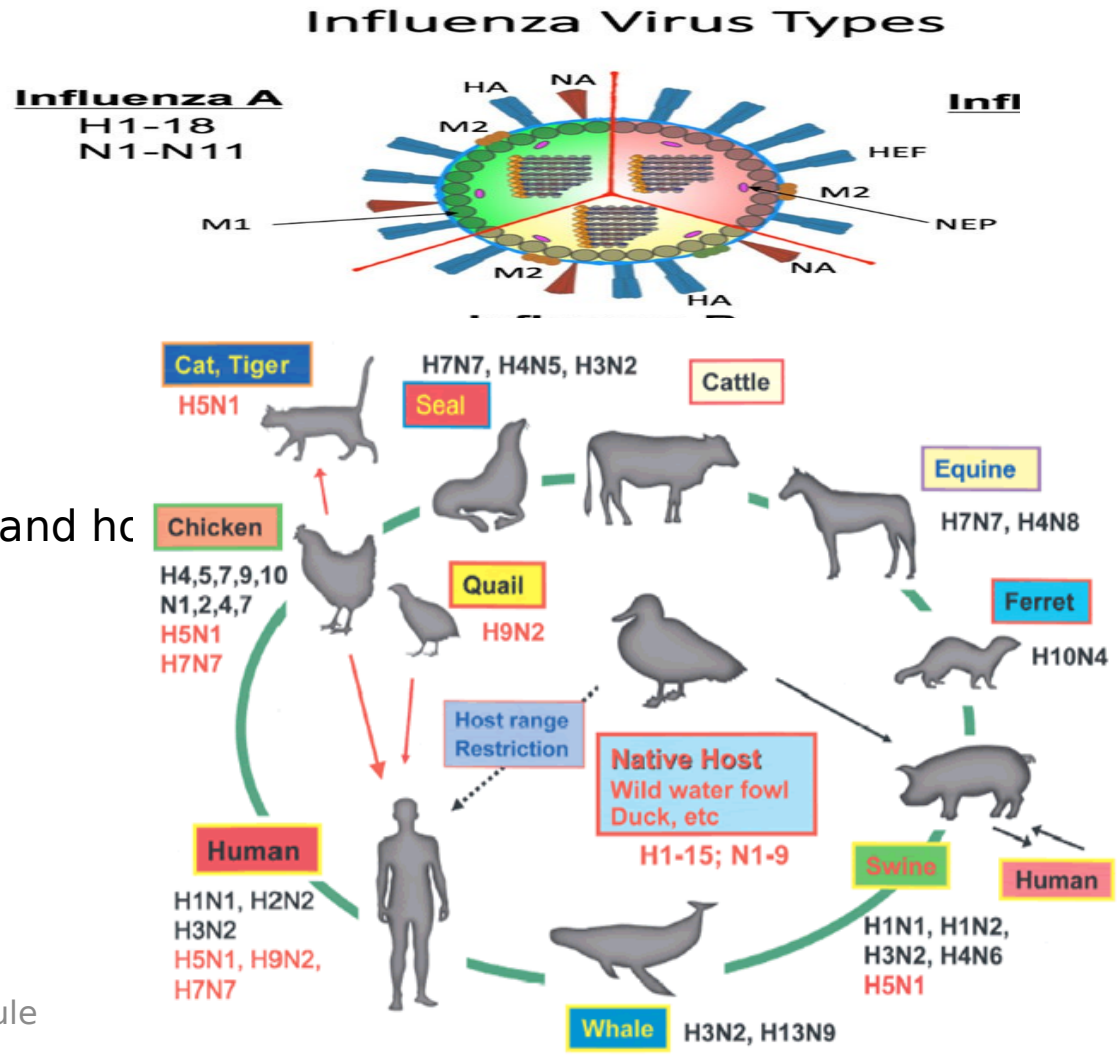
  have **their own influenza A viruses**.

- Are the **usual cause of epidemics**

Influenza B

- is only a **human** virus.
- Cause less severe disease and **smaller outbreaks**

Influenza C



Antigenic variation of Influenza viruses

Antigenic drift

- Type **A & B**
- **Spontaneous point mutation**

Minor change in amino acid sequence of **HA or NA**

(remains same strain)

Antigenic shift

- Type **A only due to wide host range** ; infects both human & animals**:** Pigs,aquatic birds & chicken
- **Genetic reassortment :** 2 viruses of different strains infect a single cell

(In pigs : susceptible to avian,human & swine strains)

Gene segment coding for **HA** or **NA** in **one** strain **is replaced by another segment from the other strain**

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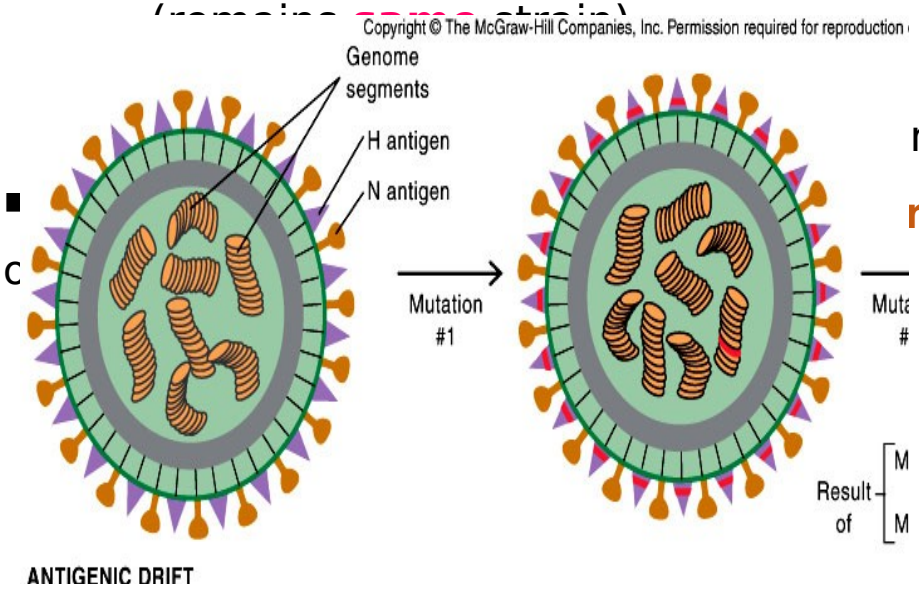
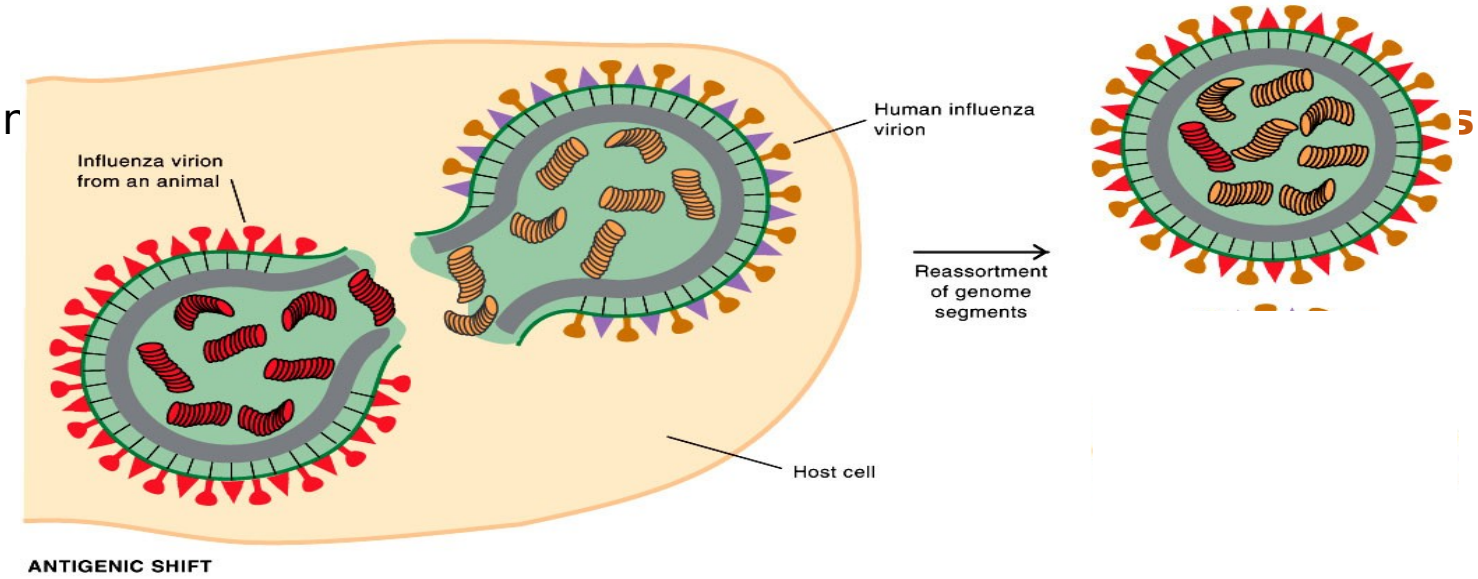
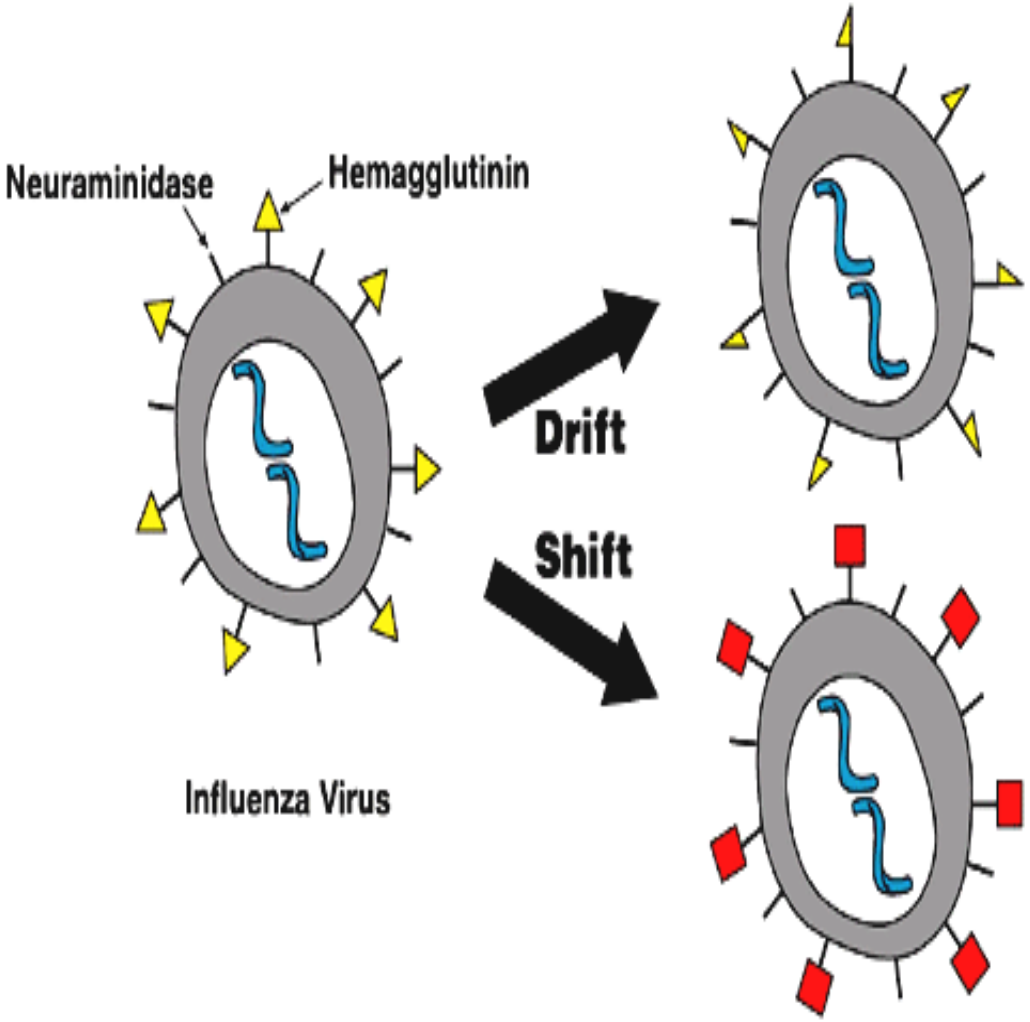
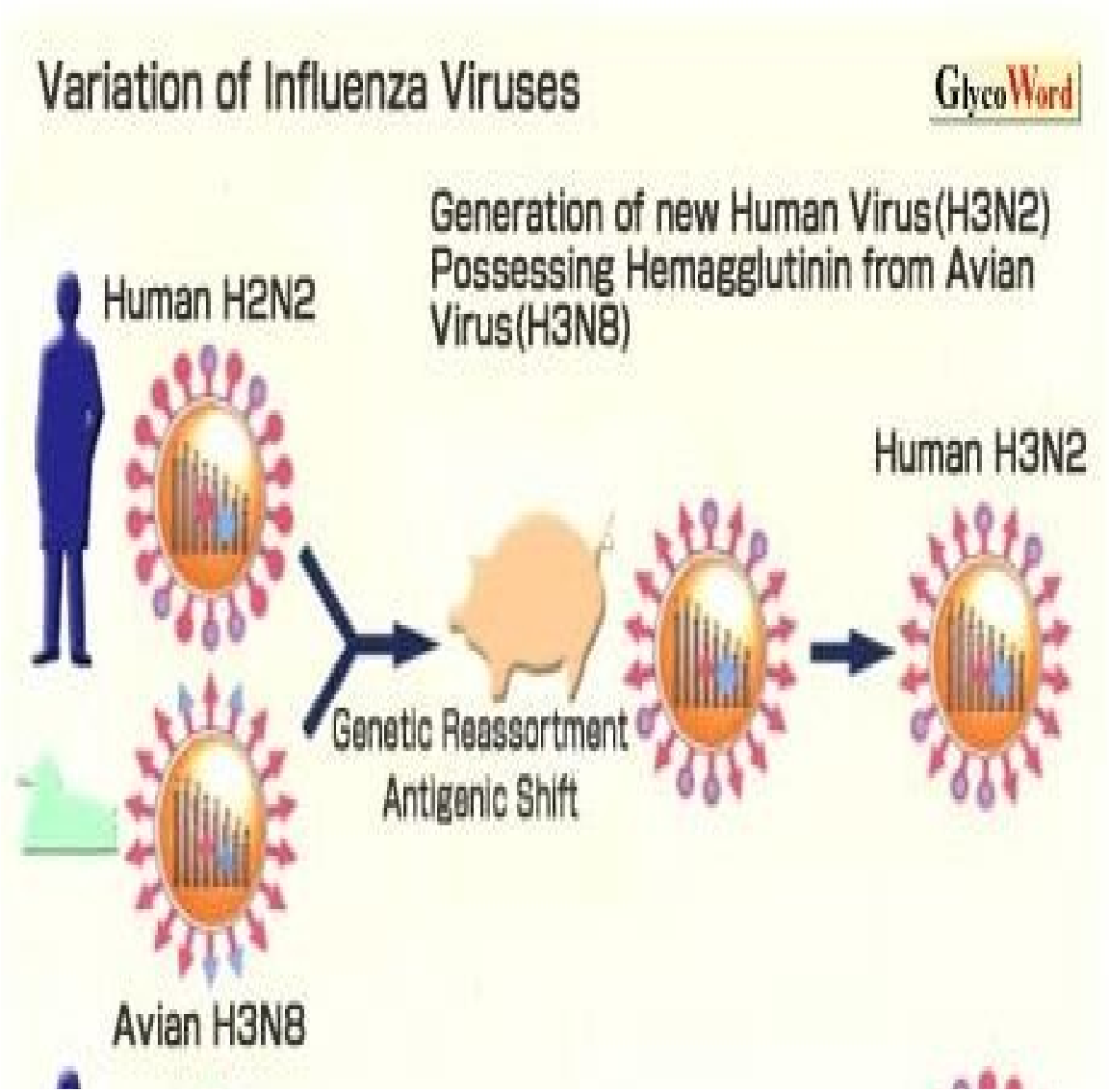





Neuraminidase
Hemagglutinin
Drift
Shift
Influenza Virus


Variation of Influenza Viruses
GlycoWord
Generation of new Human Virus(H3N2) Possessing Hemagglutinin from Avian Virus(H3N8)
Human H2N2
Human H3N2
Genetic Reassortment
Antigenic Shift
Avian H3N8

Influenza Viruses

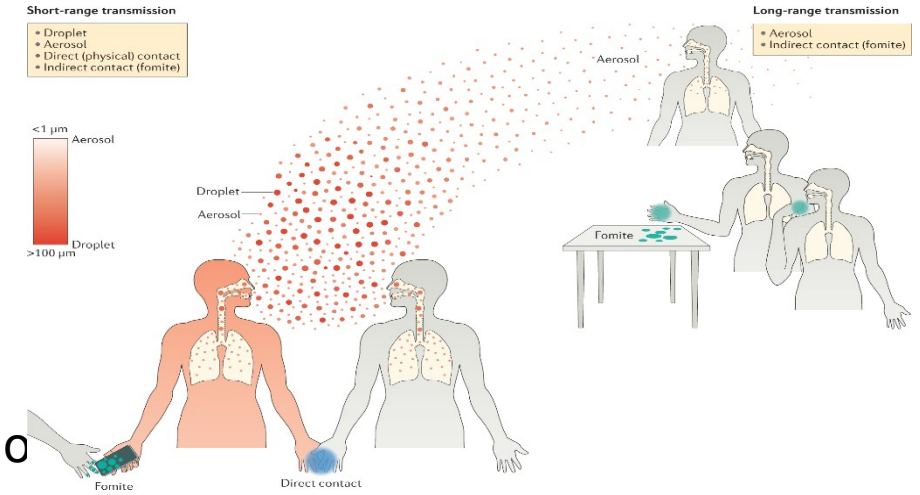
A – Mode of transmission

1- Inhalation : droplets

2-Contact :

a-Direct : hand to hand contact followed by rubbing the no

b-Indirect *:* via fomites, towels, contaminated surfaces



Influenza Viruses

B-Replication

- **NA degrades protective mucin layer** over epithelial cells of RT

  ⇩

  Virus **attachment by HA**

  ⇩

  Necrosis & desquamation of the superficial layers of resp. epith

- Infection is limited to RT as **local extracellular protease cleaves**

  ⇩

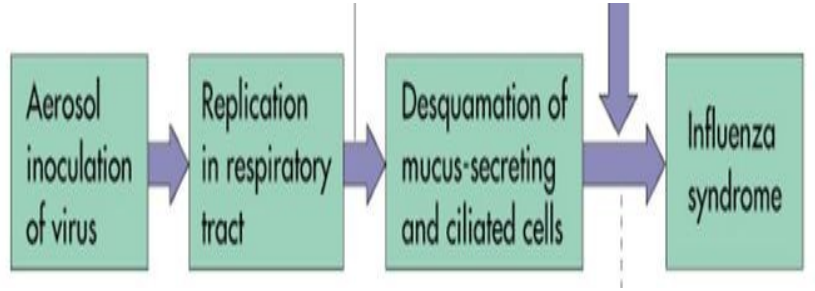
  Modified(active) HA

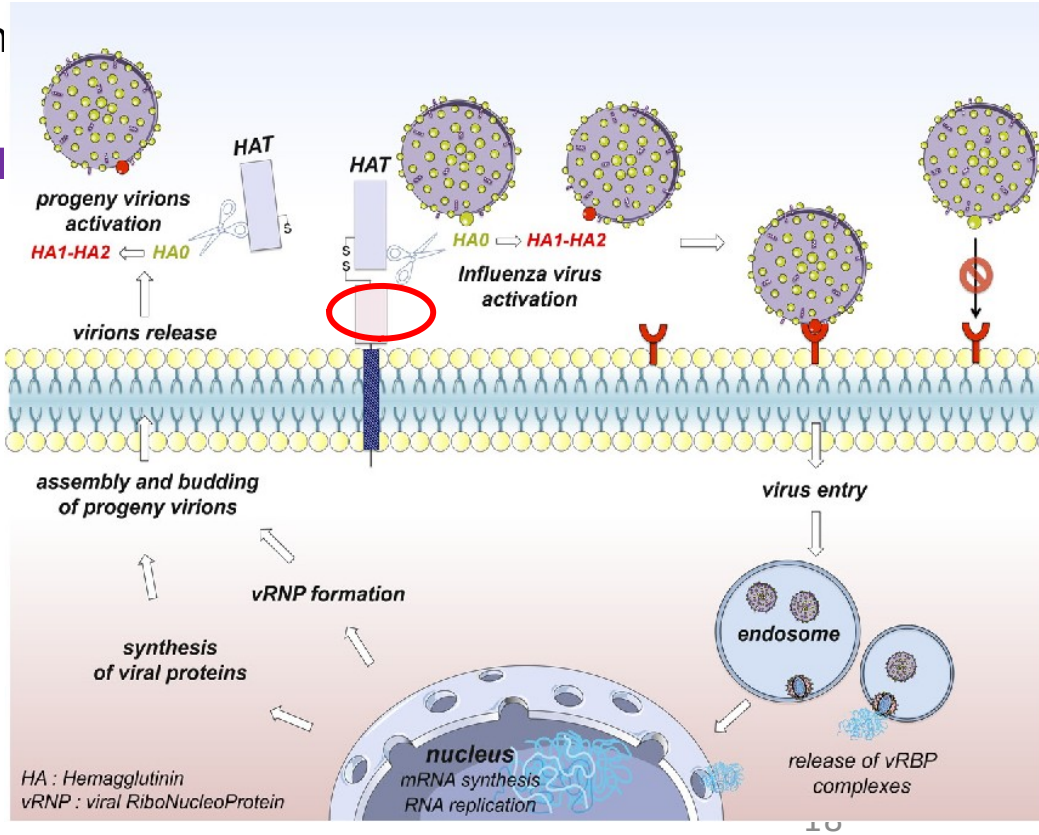
  ⇩

  Attachment to host cell

- **Systemic symptoms** are due to **cytokine** release

  (viremia is rare)

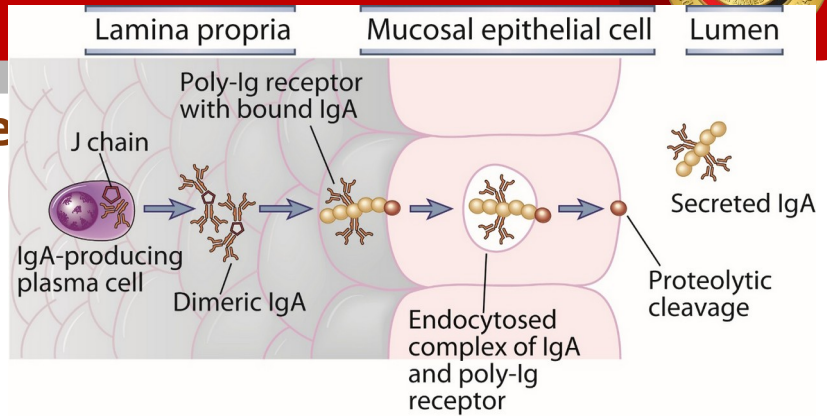




Influenza Viruses

C- Immunity

Interferon α & Secretory IgA are the main protective immunity



Clinical manifestations

A-Local : ♦Nasal discharge ♦Dry c

B-Systemic : ♠Fever,headache ♠Myalg

C - Complications: (infants, elderly, pregna

1-Otitis media (children) , & sinusitis

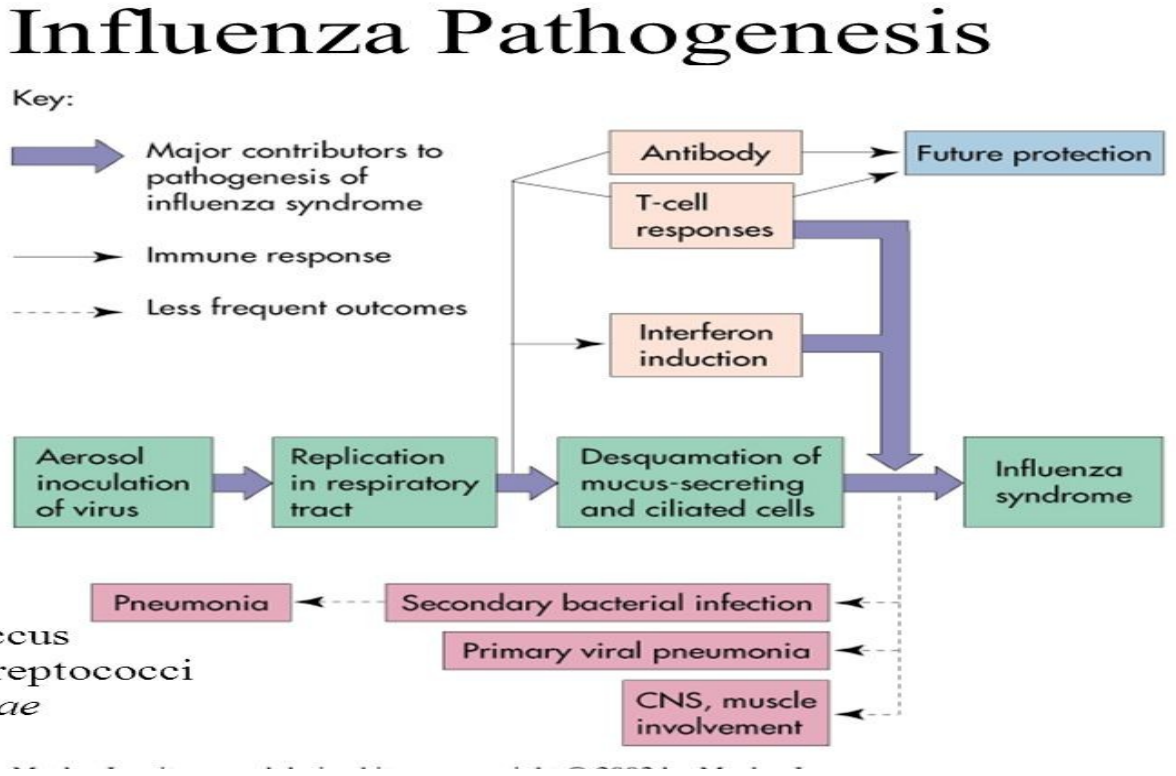
2- Bronchitis

3-Pneumonia

a.1ry viral pneumonia

b.2ry bacterial pneumonia (most com

by S.aureus☻Pneumococci



Examples of Influenza Viruses in Humans

Influenza A : H5N1 ((Avian flu)

Pathogenesis

A - Mode of transmission

1- Direct spread from chicken

2-**Rare** human to human spread

B- Replication Infect chicken & other birds more effectively than humans (W

1- Viral receptor is present **throughout the chicken RT**

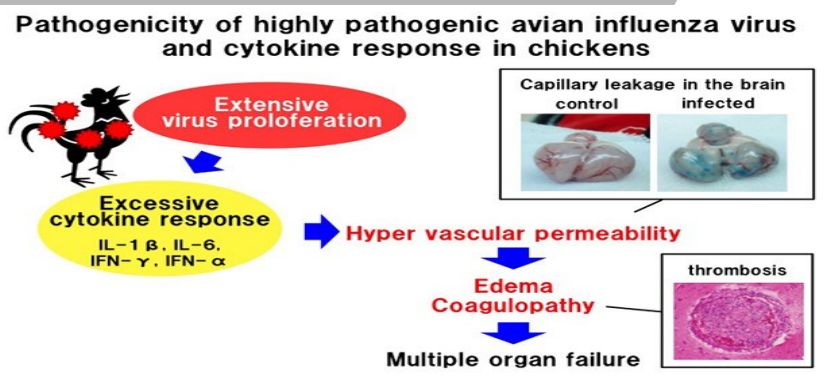
Primarily cause avian influenza **in chicken**

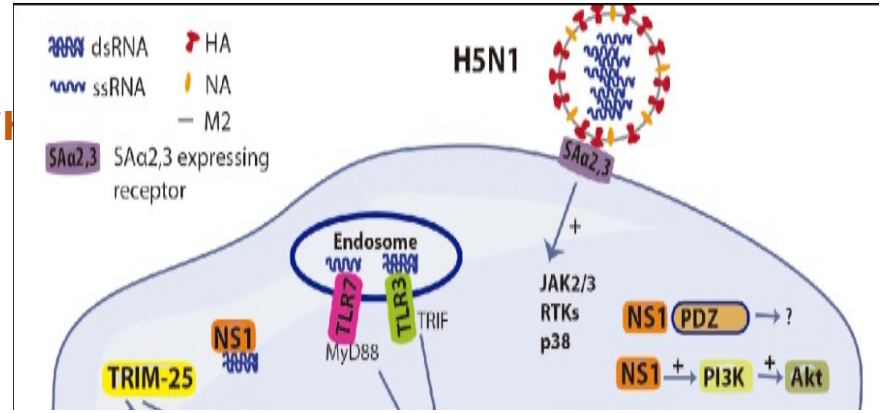
2-Viral receptor in ***human is present only in alveoli***

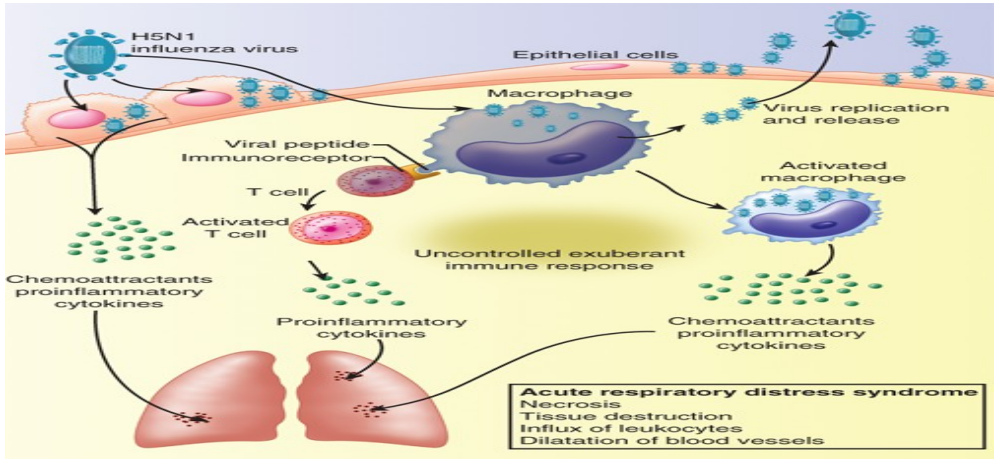
*Humans **are rarely** infected*

Extensive exposure → Virus can reach alveoli → **Severe pneumonia**

Prevention : **No vaccine** is available







Influenza Viruses

Laboratory diagnosis: for epidemiological purposes

Specimen

Nasal or throat swab

A- Rapid diagnosis

Allow initiation of treatment within 48 hours

1-ELIDA : Detection of viral Ag

2-PCR

B-Serology

Rising titer of IgG

Influenza Viruses

Prevention

A - Immunoprophylaxis: vaccination

Most reliable method for prevention

1-Contents

Quadrivalent vaccine : most recent isolates of

H1N1, H3N2 + 2 B strains

Reformulated every year to contain current antigenic strains

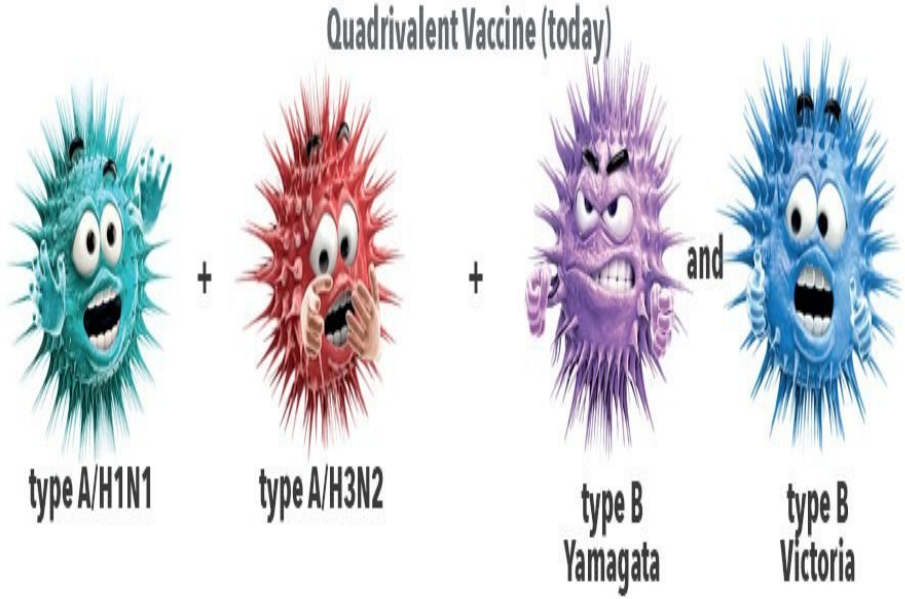
2-Effect & Administration : needs to be given every year due to

a- Short lived protection

b- Antigenic **drift**

3-Types

- **Killed (Inactivated)**
- **Live attenuated**



Inactivated (killed)

Intramuscular

In **chick embryo**

Indications

Persons with **↑ risk to develop complications & their contacts**

i.Extremes of age

ii. Immunocompromized patients

Live attenuated

Intranasal (Nasal spray)

Secretory IgA

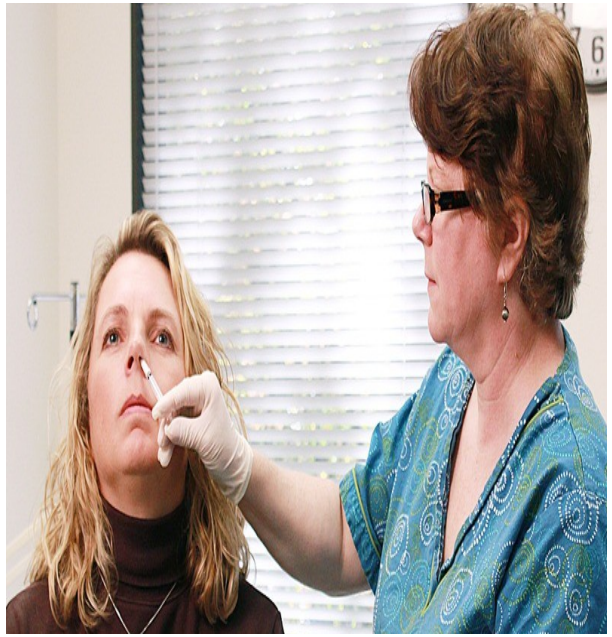
■Temperature sensitive mutants in chick embryo

Can replicate in **cold nose (33C)**

No replication in lower RT (37C)

Indications

Healthy individuals with no risk for complications



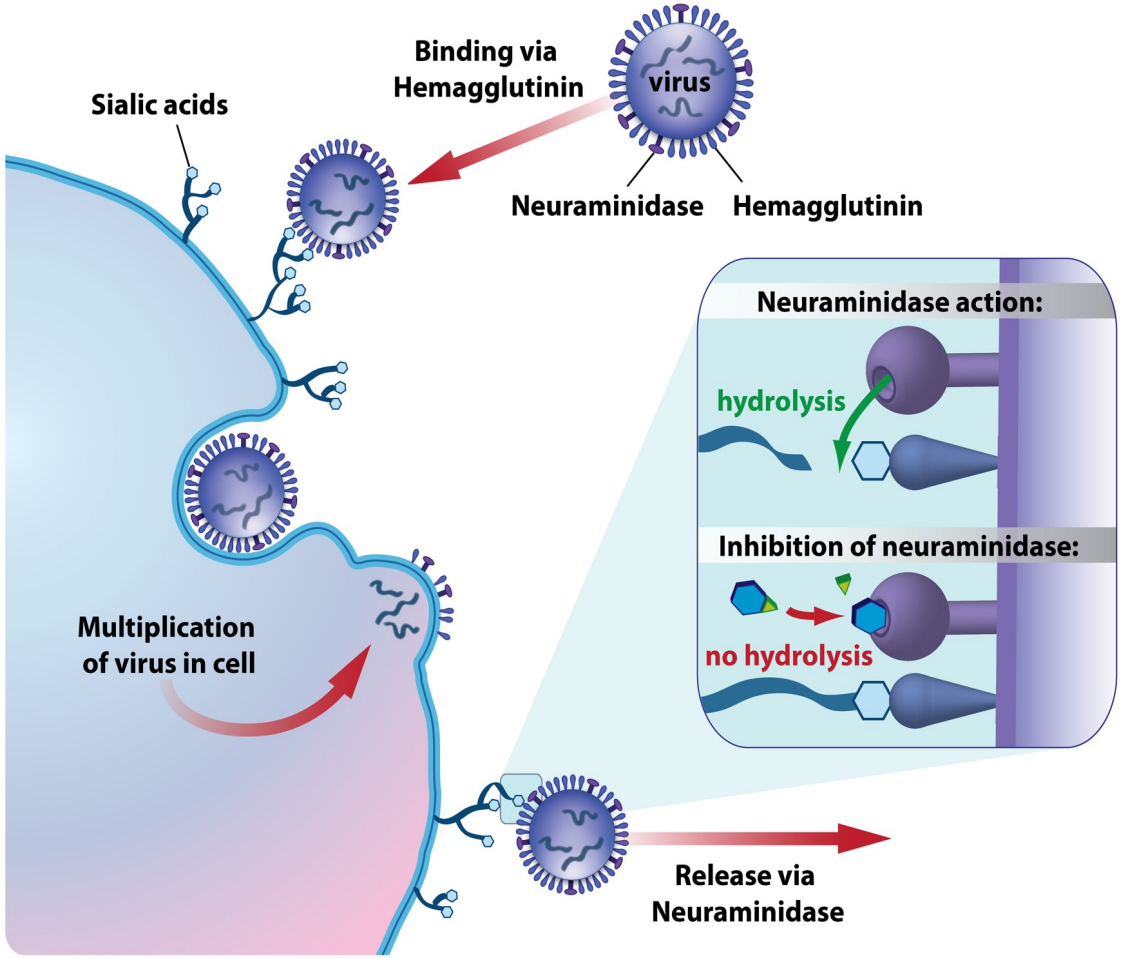
Influenza Viruses

B -Chemoprophylaxis

Neuraminidase inhibitors (oseltamivir)

Active against influenza types **A and B**

Given to exposed non vaccinated elderly



Hantavirus

Structure

A- Family

Bunyavirus

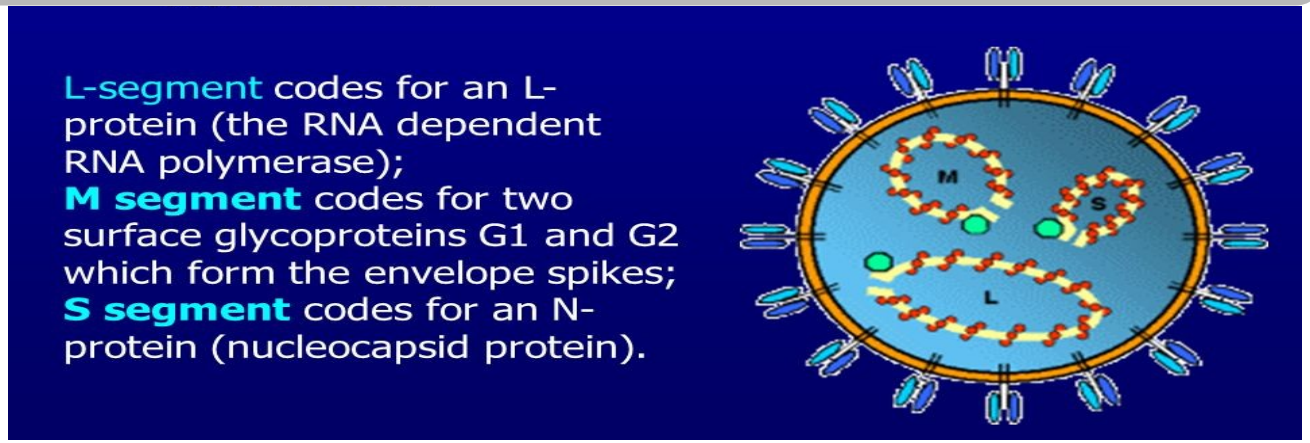
B-Nucleocapsid

ssRNA

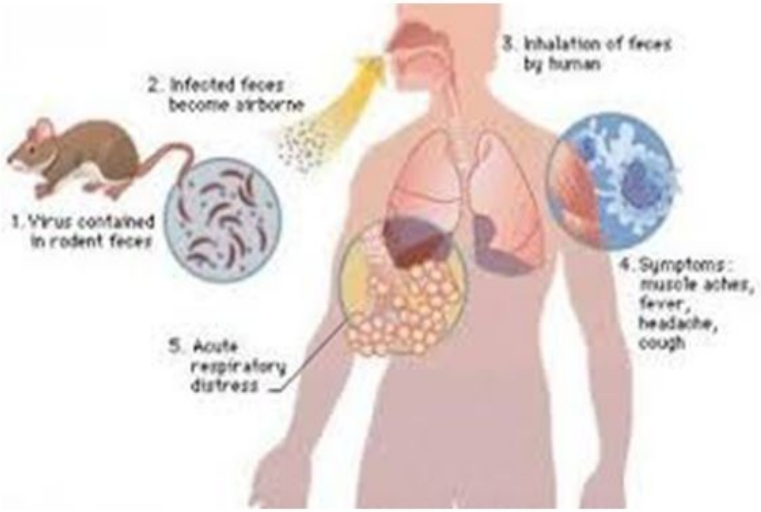
C- Enveloped

D- Sin Nombre virus

A new hantavirus that causes a severe disease called **hantavirus pulmonary syndrome (HPS).**



- Also known as Four Corners Virus or Sin Nombre Virus
- Spread through infected rodents and their excretory waste
- Deadly pulmonary disease



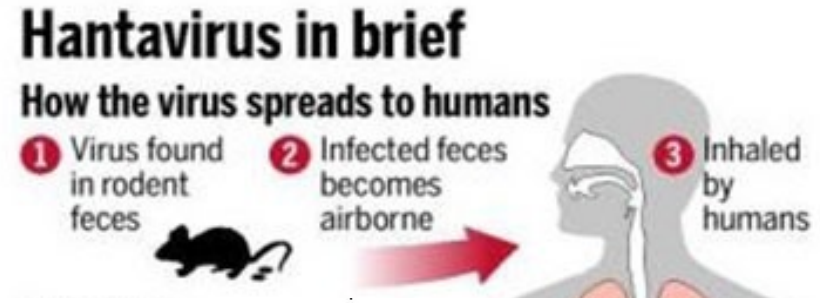
Pathogenesis

A-Mode of transmission

●**Robovirus :** transmitted from **rodents**

Inhalation of aerosols from excreta (urine, feces, or saliva) of infected dee

● **No human to human transmission**



B- Site of replication & **Effect on cells**

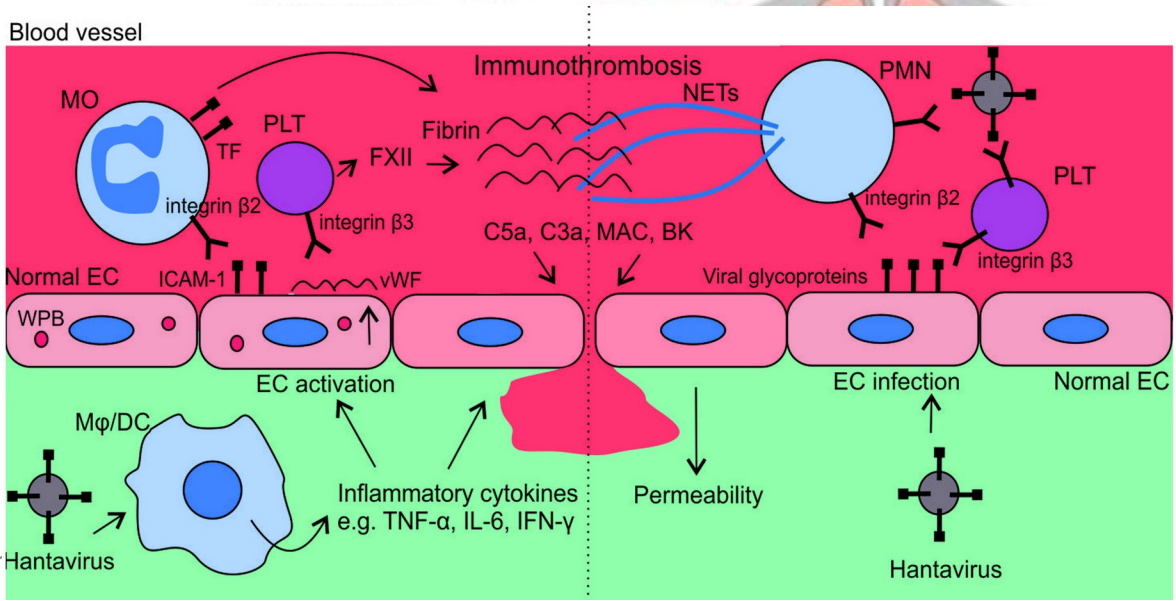
1-Virus enters the blood & travels throughout the body

Infects endothelial cells of blood capillary walls.

2- Induces release of inflammatory mediators

Leakage of fluid from capilleries

Hypotension, **pneumonia** & shock.



Hantavirus

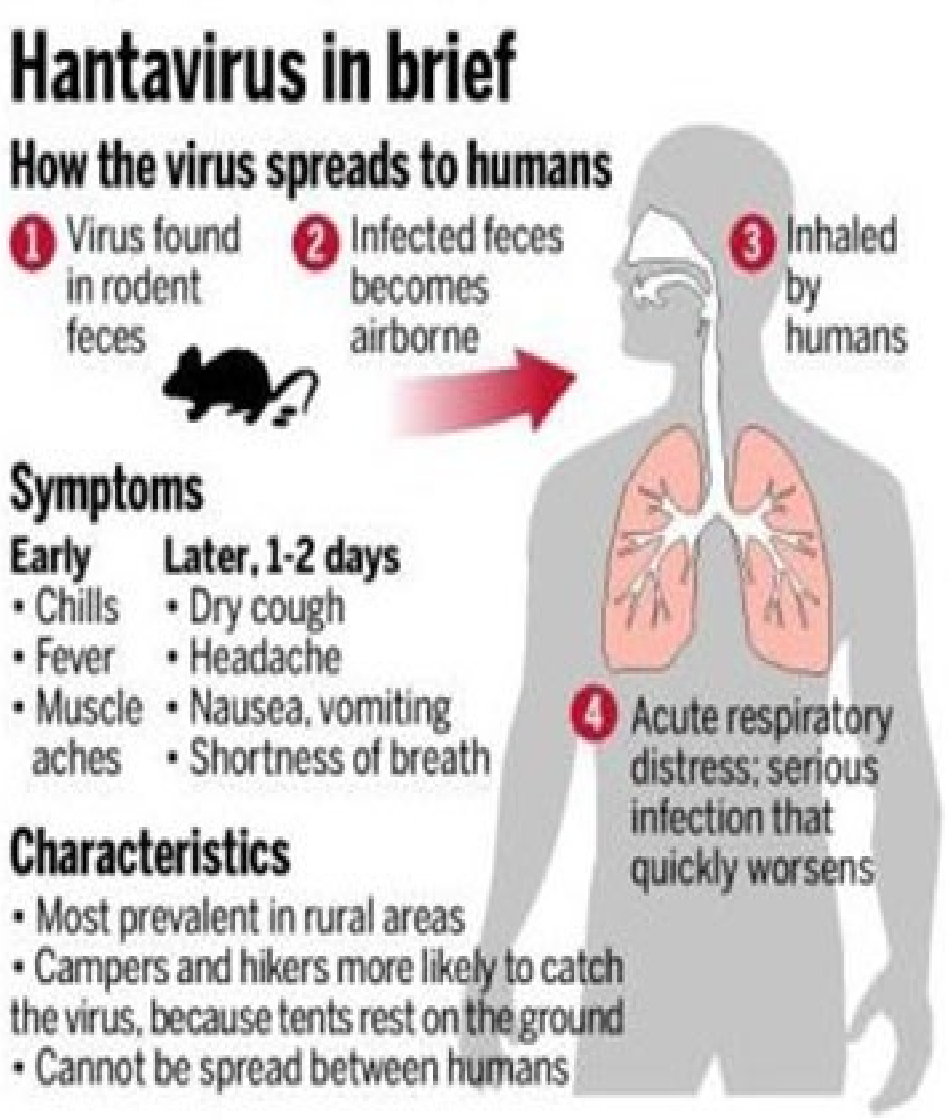
Clinical manifestations

A-Korean hemorrhagic fever (KHF)

- Petechial hemorrhage
- **Shock**
- **Renal failure**

2-Hanta pulmonary syndrome (high mortality)

- **Dry cough,pulmonary edema,**shortness of breath
- Acute respiratory failure



Hantavirus

Laboratory diagnosis

1-PCR **:**Detection of **RNA** in lung tissue

2-Serology : detection of **IgM**

Prevention

Eliminate or minimize contact with rodents by:

Seal up holes, trap & clean up food sources

SUGGESTED TEXTBOOKS

- ***Review of Medical Microbiology and Immunology, Warren Levinson pages 683-694.***

- **https://www.cdc.gov/ HAI .**

- **American Journal of Respiratory Critical Care Medecine Vol 171. pp 388–416, 2005)**

- **http://text.apic.org/item37/chapter36pneumonia/all**


Thank You